Local Cerebral Blood Volume Response to Carbon Dioxide in Man

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AND BARBARA UZZELL

SUMMARY We used an emission tomographic brain scanner to investigate the relationship between local cerebral blood volume (LCBV) and arterial blood carbon dioxide tension (Paco2) in normal awake man. Measurements were made separately in three dimensions in various regions of grey and white matter, and the resting LCBV as well as the difference in sensitivity among these regions were compared. Over the range of Paco2 studied (20–42 torr), the response of both the grey matter and the white matter to carbon dioxide was linear. The LCBV sensitivity of the grey matter to changes in Paco2 was 0.053 ml/100 g per torr Paco2 and in the white matter this sensitivity was 0.046 ml/100 g per torr Paco2. These sensitivities were found not to be significantly different, yielding a slope of 0.049 ml/100 g per torr Paco2 for the LCBV-Paco2 curve for the entire brain. This is in excellent agreement with the other data for the whole brain. The resting cerebral blood volume of the grey matter at a Paco2 of 34.4 torr, which was the average resting arterial carbon dioxide tension of the subjects, was 5.0 ml/100 g and was significantly higher than for white matter, which was 3.6 ml/100 g. At the local level, the cerebral blood volume of the frontal cortex is significantly less than that of the thalamus, whereas the frontoparietal cortex in the region of the sylvian fissure has a local cerebral blood volume significantly greater than that of the thalamus.

CEREBRAL blood volume (CBV) has been used as a measure of cerebral hemodynamics in the study of the cerebral vasculature. Due to the difficulty in measuring cerebral blood volume experimentally, there is not a great amount of data examining its relationship to alterations in the physiological state. In particular, the correlation between cerebral blood volume and arterial carbon dioxide tension (Paco2) lacks extensive documentation. Smith et al.1 calculated CBV from measurements of cerebral blood flow and mean cerebral transit time. These measurements were of global CBV only. To obtain regional or local cerebral blood volume (LCBV), Ter-Pogossian et al.2 and Phelps et al.3 used an x-ray fluorescence technique to examine the local cerebral blood volume response to alterations in arterial carbon dioxide tension in rhesus monkeys. This method, however, allows measurement of LCBV in only one region of the brain at any one time.

To circumvent this problem, Kuhl et al.4 developed a technique using emission tomography and 99mTc-labeled red blood cells that is capable of measuring LCBV simultaneously in multiple regions of the brain with a resolution of 1.7 cm. An entire transverse section scan can be made in less than 5 minutes. With this technique, LCBV response to alterations in Paco2 was obtained in a series of baboons. We have employed this emission tomographic method to measure the LCBV response to carbon dioxide in a series of normal human volunteers.

Methods

Ten male volunteers (18–22 years) were studied. Institutional and HEW resolutions for the protection of human subjects were obtained. With the subject lying comfortably on the scan table, a short catheter was inserted in the left (for right-handed subjects) brachial artery after pretreatment of the injection site with a local anesthetic. This catheter was joined through an Intraflo (Sorenson Research Co.) continuous flush system to a pressurized saline bag containing 1 U of heparin/ml which allowed a slow (3 ml/hour) flow through the catheter to prevent clotting. Also attached to the Intraflo was a Statham blood pressure transducer. After catheterization, the subject’s head was placed in a foam cast that previously had been fabricated individually to fit the subject snugly and prevent head motion. This cast then was placed into the center of the detector assembly of the Mark IV scanner which was used to obtain the transverse section scan.5 The lumen of the catheter was connected to two-way respiratory valve the input of which was joined to an air bag. The air bag could be filled with the desired gas mixture from prepared, premixed gas cylinders. The subject’s tidal carbon dioxide concentration was monitored with an infrared CO2 analyzer (Beckman Instru-
ments—LB2) and recorded, along with blood pressure, on a Hewlett-Packard polygraph.

With the subject comfortable, 20 mCi of 99mTc-labeled red blood cells were injected into the subject's arm vein. This tracer was produced by drawing 10 ml of venous blood from the subject approximately 1 hour previous to this time and labeling the red blood cells with 99mTc.

Protocol
Approximately 15 minutes after the injection of 99mTc-labeled red blood cells, the study began. Two separate protocols were used, with five subjects included in each. In protocol A, the first two scans were obtained with the subject breathing room air. These two scans were made as close together as was possible (usually less than 1 minute elapsed between the end of the first scan and the beginning of the second scan). Following the second scan, the inhalation mixture was switched from room air to a mixture of 3% CO₂ and 21% O₂ with the balance N₂; the subject breathed this gas mixture for 10 minutes. Then the third scan was obtained. The inspired gas then was changed to 5% CO₂, 21% O₂ with the balance N₂. The subject breathed this for 10 minutes preceding the next scan (scan number 4). At this point the respiratory tubing was disconnected from the valve at the subject's mouth-piece and he was instructed to hyperventilate to bring his end-tidal carbon dioxide concentration (ETCO₂) down to between 3.0% and 3.2%. This end-tidal CO₂ concentration was displayed on a large analog meter placed above the scanner in clear view of the subject. With the aid of visual feedback from this meter, the subject was instructed to keep his end-tidal CO₂ concentration steady at this level until after the next scan. The subject hyperventilated for 10 minutes and then brain scan number 5 was obtained. Following this scan, the subject was instructed to breathe normally, and brain scan number 6 was obtained after his end-tidal CO₂ concentration had been stable for 10 minutes at a value close to that of the first two (room air) scans.

Protocol B was identical to protocol A except that the order of CO₂ administration and hyperventilation was reversed. Thus the scan sequence was: scan numbers 1 and 2, room air; scan number 3, hyperventilation to 3.0–3.2% ETCO₂; scan number 4, 3% CO₂; scan number 5, 5% CO₂; scan number 6, room air breathing.

Throughout each scan a number of blood samples were drawn from the indwelling arterial catheter. At the beginning of the scan, 7–8 ml of blood were drawn for analysis of 99mTc activity in the blood at scan time. This was followed immediately by two 1-ml blood samples for analysis of PCO₂, PO₂, and pH. Toward the end of the scan, two additional blood samples were taken for PCO₂, PO₂, and pH determination, the mean of the four samples determining the blood gas status of the subject during the particular scan. Blood gas was analyzed with appropriate electrodes at 37°C, corrections being made for glycolysis during the time between obtaining the blood sample and performing the analysis.

LCBV was calculated by the methods outlined previously. All scans were obtained approximately 5 cm above the orbital-meatal line. A scan was comprised of five revolutions of the detector assembly around the subject's head for a total scan time of 250 seconds. This produced approximately 750,000 total counts in a picture, and this has been shown by Kuhl et al. to be necessary for a statistically satisfactory scan. The subject was instructed to keep his head still throughout the entire procedure, which lasted about 90 minutes. The volumes of tissue examined (both grey and white matter) were considered large enough for the hematocrit to be assumed equal to the average hematocrit for the whole brain (0.85 X peripheral venous hematocrit).

Data Analysis
The output of each scan was a 64 X 64 matrix array of the reconstructed counts. For ease of analysis, this was reduced to a 32 X 32 array which also was output on a computer display oscilloscope as a local cerebral blood volume picture. Regions of interest in this picture were identified on a neuroanatomic basis, and the corresponding local cerebral blood volume was obtained from the 32 X 32 array by multiplying the counts in the region by appropriate scale factors representing, among other factors, radioactive decay (from the time of isotope injection). These cerebral regions were identified neuroanatomically, and efforts were made to analyze the same structures in all the subjects.

Three grey matter areas were selected for analysis. They were the thalamus, the frontal cortex, and the insular cortex in the region of the sylvian fissure. The white matter areas examined were the frontal white, internal capsule, and occipital white. In Figure 1, a typical reconstructed scan and the areas of interest are shown. The local blood volume of each area was obtained by averaging the counts in at least 20 picture elements for a total cross-sectional area of approximately 3.2 cm². These measurements usually were obtained in both hemispheres so that the regional cerebral blood volume of each region was based on a cross-sectional area of at least 6.4 cm². For a given cerebral region, only the most central pels in that region were used, to minimize possible contamination of adjacent tissues. Thus the blood volume of the thalamus was obtained using pels only in the central region of the thalamus to minimize contamination by the surrounding white matter. For analysis of some of the data, all of the grey matter structures examined were averaged together and taken to be representative of the cerebral grey matter; the white matter structures were averaged and taken as representative of cerebral white matter.

Results
In all of the subjects, inhalation of carbon dioxide caused an increase in cerebral blood volume and moderate hyperventilation caused a decrease in cerebral blood volume from the normal levels. This can be seen in Figure 2, where cerebral blood volumes of both the grey and the white matter are plotted as a function of arterial carbon dioxide tension for each subject. Although these data do exhibit some scatter, especially in the absolute value of blood volume between subjects at a given arterial carbon dioxide tension, the response to CO₂ of the individual subjects is very consistent. The LCBV response to CO₂
appears linear; a polynomial regression of degree higher than first order is not a statistically significant improvement as a representation of these data. The linear regression parameters are tabulated for each subject in Table 1.

Five of the subjects were asked to hyperventilate prior to the CO₂ administration (protocol B) and the other five subjects hyperventilated after CO₂ administration (protocol A). These are indicated in Table 1. To see if the order of study influenced the results, both the slope and the constant of the linear regression were examined for statistical differences between the two groups using a paired "t" parameter. No significant difference in the sensitivity of cerebral blood volume to alterations in carbon dioxide was found. This indicates that all 10 subjects could be examined together without regard for the order of study.

To examine more clearly the sensitivity of cerebral blood volume to changes in arterial carbon dioxide tension, the data were normalized around a control carbon dioxide tension. This control P_{CO₂} (34.4 torr) was obtained by averaging all the subjects' arterial carbon dioxide tensions for the first two scans when the subject was breathing only room air. With the regression equation for each individual subject, a local cerebral blood volume was obtained at this control P_{CO₂}. The local cerebral blood volumes measured in each subject were divided by this baseline control blood volume to compute a normalized local cerebral blood volume. This procedure removes the baseline blood volume differences that were present.
Table 1

<table>
<thead>
<tr>
<th>Subject</th>
<th>a</th>
<th>b</th>
<th>LCBV</th>
<th>a</th>
<th>b</th>
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<td>3.26</td>
<td>4.44</td>
<td>0.040</td>
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<td>3†</td>
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<tr>
<td>4†</td>
<td>0.055</td>
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<td>6.10</td>
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<td>0.039</td>
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</tr>
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<td>0.060</td>
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<td>0.059</td>
<td>1.13</td>
<td>3.16</td>
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<td>5.60</td>
<td>0.038</td>
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<td>3.53</td>
<td>4.97</td>
<td>0.036</td>
<td>2.97</td>
<td>3.26</td>
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</table>

Mean 0.053 3.19 5.02 0.046 1.76 3.55
SE 0.0056 0.24 0.192 0.004 0.19 0.077

The relationship between local cerebral blood volume (LCBV) and arterial carbon dioxide tension (Paco2) in the range 20-42 torr for each subject for both grey and white matter. The coefficients (a, b) of a linear regression (LCBV = aPaco2 + b) performed on data of each subject are tabulated along with LCBV obtained from this regression at Paco2 = 34.4 torr which was the average arterial carbon dioxide tension of all subjects breathing room air.

* Hyperventilated prior to CO2 administration.
† Hyperventilated following CO2 administration.

Heterogeneity of Cerebral Blood Volume

Table 1 summarizes the individual linear regression coefficients for each subject describing the relationship between local cerebral blood volume and Paco2 for both grey matter and white matter. The average regression equations are:

\[ \text{LCBV} = 0.053 \text{Paco2} + 3.19 \text{ (grey matter)} \]
\[ \text{LCBV} = 0.046 \text{Paco2} + 1.76 \text{ (white matter)} \]

where coefficients are the means of the respective slopes and intercepts of the individual subjects. A paired t test using these individual coefficients does not show any significant difference between the slopes of the two regression equations. Consequently, the sensitivity of local cerebral blood volume to arterial carbon dioxide alterations is not different for grey and white matter. We thus can average them to obtain a mean blood volume sensitivity of cerebral tissue to carbon dioxide of 0.0495 ml/100 g per torr PaCO2. The intercepts of the two regression equations are significantly different (P < 0.001), indicating a difference in baseline cerebral blood volume between grey matter and white matter. This difference can be determined more meaningfully by examining the local cerebral blood volumes at a typical arterial carbon dioxide tension. Cerebral blood volumes at PaCO2 = 34.4 torr are tabulated in Table 1; the mean cerebral blood volume of grey matter (5.02 ml/100 g) is significantly greater than the mean cerebral blood volume of white matter (3.55 ml/100 g) (P < 0.001).

The specific areas comprising both grey and white matter also were analyzed for differences in both baseline blood volumes and blood volume response to carbon dioxide. Among the grey matter structures, there were no significant differences in sensitivity to arterial carbon dioxide alterations. There were, however, statistically significant differences in the baseline cerebral blood volumes of the three areas at a control carbon dioxide tension level of 34.4 torr to unity and scaling all blood volumes accordingly (see text). The grey matter (A) and white matter (B) are shown separately.
Table 2  Reproducibility of LCBV Determinations

<table>
<thead>
<tr>
<th>Subject</th>
<th>LCBV scan no. 1</th>
<th>LCBV scan no. 2</th>
<th>Adjusted LCBV (grey) no. 2</th>
<th>Adjusted LCBV (white) no. 2</th>
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<tr>
<td>1</td>
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<td>5.44</td>
<td>5.01</td>
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<td>4.88</td>
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<td>4</td>
<td>6.29</td>
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<td>6</td>
<td>4.09</td>
<td>4.32</td>
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<td>4.63</td>
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<tr>
<td>8</td>
<td>5.54</td>
<td>5.71</td>
<td>5.66</td>
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<tr>
<td>9</td>
<td>4.99</td>
<td>5.10</td>
<td>5.10</td>
<td>3.54</td>
</tr>
<tr>
<td>10</td>
<td>4.93</td>
<td>4.94</td>
<td>4.95</td>
<td>3.31</td>
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</table>

P < 0.001 level. The white matter areas (frontal white, internal capsule, and occipital white) exhibited neither differences of cerebral blood volume sensitivity to CO₂ nor differences in baseline (Paco₂ = 34.4 torr) local cerebral blood volume.

Reproducibility of Technique

The protocol for all 10 subjects included two initial sequential section scans while breathing room air. Consequently, there was minimal change between the two scans in arterial carbon dioxide tension, head position as well as other physiological parameters. These back-to-back scans yield data on the reproducibility of the entire tomographic scanning technique for measuring local cerebral blood volume in man. Those data are shown in Table 2. The coefficient of variation of LCBV in this test-retest situation was 4.3% for grey matter and 3.0% for white matter. If the blood volumes obtained from the second scan are corrected for slight changes in the arterial carbon dioxide tension that occurred between the two scans, the coefficients of variation become 3.4% and 2.9% for grey and white matter, respectively.

Discussion

There is a variety of methods for cerebral blood volume measurement. One technique involves injecting ¹³¹I-labeled serum albumin (RISA) into the blood. Approximately 1 hour later a blood sample is drawn, the animal killed, the brain frozen, and a representative brain tissue sample obtained. The ratio of the counts per minute per unit volume in the brain sample and the blood sample yields the blood volume. A similar technique uses ⁵¹Cr-labeled red blood cells as the tracer. Sklar et al. obtained a cerebral blood volume in cats of 2.7 ml/100 g using RISA and 1.9 ml/100 g using ⁵¹Cr-labeled red blood cells. These values are significantly lower than those reported by Weil et al. who measured the brain content of silver following an intravenous injection of a hypertonic solution (collargol) in dogs. Their value of 8.3 ml/100 g differs from that of Sklar et al. probably because of differences in methodology and species. These techniques, however, do not lend themselves to measurements in man, nor can repeat volume determinations be made.

The red cell-labeling technique was modified for use in man by estimating the concentration difference of ³²P-labeled erythrocytes across the brain from samples of carotid arterial and jugular venous blood following an intravenous injection of the tracer. This technique measures total brain blood volume. Assuming the brain weight to be approximately 1400 g, the cerebral blood volume obtained was 7.0 ml/100 g.

Risberg et al. modified the RISA method of blood volume determination to measure regional cerebral blood volume using external scintillation detectors. An interval of approximately 80 minutes was allowed for equilibration following an intravenous injection of 1–2 mCi of ¹²⁵I-labeled serum albumin in cats. Knowledge of the volume seen by each probe as well as the arterial blood RISA activity allows calculation of regional cerebral blood volume. When the brain was removed with minimal blood loss, the extracerebral background blood pool was found to comprise approximately 30% of the measured blood volume. Absolute values of blood volume are not reported. This technique is an improvement over the in vitro methods in that it can be used in man, but suffers from the limitation of not being totally regional. Additionally, the cerebral blood volume measurement is contaminated by extracerebral contributions. Similarly, Matthews et al. calculated cerebral blood volume in man from cerebral blood flow measured by the intracarotid ¹³⁢³Xe injection technique and from the mean cerebral transit time using ⁹⁹mTc pertechnetate. These measurements were made with a gamma camera and so regionality was obtained.

In order to obtain three-dimensional resolution of cerebral blood volume in man, Ter-Pogossian et al., Phelps et al., and Grubb et al. developed a technique whereby the characteristic x-ray fluorescence of iodine from an injected contrast material is excited with a narrow (1 cm in diameter) x-ray beam. The resulting fluorescence is detected with a collimated radiation spectrometer. The intensity of the signal is proportional to the amount of label in the region of study. By placing a sample of the subject’s blood in a phantom, this instrument can be calibrated and an absolute value of local cerebral blood volume calculated. Using this technique, these investigators obtained a value for local cerebral blood volume in man of 3.2 ml/100 g tissue. Their reported values for the dog and monkey are slightly higher. The major disadvantage of this technique is that cerebral blood volume can be measured only in one region of the brain at a time. Furthermore, since the contrast agent does not stay in the intravascular compartment in certain pathological conditions in which there is an altered blood brain barrier (meningioma, glioblastoma, etc.), this technique will overestimate local cerebral blood volume in these areas.

This objection has been circumvented by Kuhl et al. who developed a method for measuring local cerebral blood volume throughout a brain section with three-dimensional resolution. They used a transverse section...
scanner (Mark III, the predecessor of the Mark IV used in this investigation) to measure the local activity of 99mTc-labeled red blood cells and studied patients as well as examined the local cerebral blood volume response of baboons to carbon dioxide. 1

Various attempts have been made to measure cerebral blood volume with a computerized transverse axial scanner. 16, 18 Such a technique would be advantageous because of the excellent resolution (1.5 × 1.5 × 13 mm) of this instrument as well as the wide availability of transaxial tomographic scanners. Two separate scans are made of the subject's head. The first is a normal scan without introduction of a contrast agent and the second section scan is obtained following the introduction of a high density contrast agent (diatrizoate sodium, 14 sodium iothalamate). The two scans are subtracted to obtain the increase in density due to blood content. Knowledge of the concentration of contrast agent in the blood allows local cerebral blood volumes to be quantitated. As was discussed for the x-ray fluorescent technique, the contrast agent crosses the blood brain barrier in pathological situations and so this technique cannot be used in disease states.

The technique used in this investigation has yielded data on local cerebral blood volume in an entire section of the human brain in vivo. The resolution of the Mark IV scanner has allowed us to obtain measurements of LCBV in grey matter and white matter separately and to quantify further the LCBV in various specific cerebral areas. The cerebral blood volume of normal resting man obtained in this study, 5.02 ml/100 g for grey matter and 3.55 ml/100 g for white matter, agrees well with the literature (Table 3). It can be seen in this table that cerebral blood volume ranges from 1.9 to 8.3 ml/100 g, depending on the study. This wide range is limited data in the literature (Table 3). It can be seen in this table that cerebral blood volume ranges from 1.9 to 8.3 ml/100 g, depending on the study. This wide range is likely due to differences in techniques and species. The cerebral blood volume of normal resting man obtained in this study is consistent with the reports of relative vascularity and with what is known about blood flow in the different cerebral tissues.

Table 3 also lists the sensitivity of cerebral blood volume to alterations in PaCO2 obtained by various previous investigations. The values obtained in this study, 0.053 ml/100 g per torr PaCO2 for grey matter and 0.046 ml/100 g per torr PaCO2 for white matter with an average whole brain blood volume of 0.0495 ml/100 g per torr PaCO2, are in excellent agreement with these prior measurements.

We can define a percentage volume change index (PVCI) as the percentage change in cerebral blood volume of the tissue for a 1-torr change in arterial carbon dioxide tension using 34.4 torr as the carbon dioxide tension for computing the percentage change. Computing PVCI for grey and white matter separately, we obtain 1.05 ± 0.11% change/torr and 1.40 ± 0.14% change/torr, respectively. Thus, PVCI is greater for white matter than for grey (P < 0.05), indicating that for a given increase (or decrease) of PaCO2, the white matter increases its blood volume by a greater percentage than does the grey matter.

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Table 3  Summary of CBV and CBV-PaCO2 Sensitivities in the Literature

<table>
<thead>
<tr>
<th>Species</th>
<th>CBV*</th>
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<th>Technique</th>
<th>Reference</th>
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<td>Cat</td>
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<td></td>
<td>^131RISA</td>
<td>7</td>
</tr>
<tr>
<td>Cat</td>
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<td>^51Cr-RBC</td>
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<td>Collargol</td>
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Cerebral blood volumes (CBV) and sensitivities of CBV to carbon dioxide in this investigation and values from the literature. CBF = cerebral blood flow, RISA = radioactive iodine-labeled serum albumin, RBC = red blood cells, t = mean transit time, ICG = indocyanine green, CAT = computerized axial tomography.

* Cerebral blood volume (ml/100 g) adjusted when possible to an arterial carbon dioxide tension (PaCO2) of 34.4 torr.
† CBV sensitivity to carbon dioxide (ml/100 g per torr PaCO2).
From the blood volume picture resulting from the section scan, a few specific cerebral regions were identified (frontal cortex, thalamus, and insular cortex in the region of the sylvian fissure). The resting blood volume of the frontal cortex (3.93 ml/100 g) was significantly smaller than that obtained for the thalamus (5.00 ml/100 g). The value for the blood volume of the thalamus is very close to that found by Ladurner et al.16 who measured local cerebral blood volume using a transmission-computerized tomographic scanner. They obtained a value of 5.1 ml/100 g with a standard deviation of 1.0 ml/100 g, whereas our value is 5.0 ± 0.64 (sd) ml/100 g. These are not significantly different. The blood volume we obtain for the frontal cortex (3.93 ± 0.52 ml/100 g) is less than that found by Ladurner et al.16 (6.3 ± 3.1 ml/100 g). This is probably due to the fact that their data were obtained in patients with a variety of brain disorders. As discussed by Phelps and Kuhl,19 transmission-computed tomography is not a valid technique for cerebral blood volume determination in pathological states. It will cause an overestimation of the measured blood volume, which may explain the high value obtained by Ladurner et al.16 in the frontal cortex. Although these investigators attempted to limit their tissue samples to the "normal" hemisphere of their patients, extrapolation of blood volumes obtained in patients with known neurological deficits to the normal individual is less than ideal. Additionally, the transmission tomographic technique requires the subtraction of two scans (a scan without a contrast agent is subtracted from a scan in which a contrast agent has been used). Since the EMI numbers of the two scans are similar, the difference is subject to considerable error. For example, in a series of 17 patients, Ladurner et al.16 obtain a mean EMI number in the thalamus of 17.7 before injection of sodium iothalamate. An error only 1.0 of an EMI number may produce an error of 50% in the computed blood volume. The technique used in our studies (radioactive labeled red blood cells detected with an emission tomographic scanner) is not susceptible to this problem.

After hyperventilation in some of the subjects the cerebral blood volume did not return to its control level in spite of a return of the arterial carbon dioxide tension to its resting value. This suggests that the cerebral vasculature may require more than 15 minutes to recover from a stimulus causing a significant decrease in blood volume. This represents a longer response time than has been found for the adjustment of cerebral blood flow to carbon dioxide alterations.20,21 This may be due to the fact that cerebral blood flow alterations are caused by active arteriolar diameter changes, whereas the mechanism for cerebral blood volume changes may include a passive component (dilation of capillaries and/or opening up of previously closed capillary beds).

It has been shown that cerebral blood volume changes are produced by alterations in arterial blood pressure.3,4 The data in this study have been analyzed for such a relationship by performing a multiple regression with arterial blood pressure and PaCO2 as the independent variables and LCBV as the dependent variable. Local cerebral blood volume and arterial blood pressure correlated poorly due in large part to the very small blood pressure changes observed in the subjects during the study. Blood pressure was altered only secondarily to alterations in arterial carbon dioxide tension. Since PaCO2 was changed only over a relatively narrow range (20–42 torr), the induced arterial blood pressure changes were small. Consequently, the correlation between local cerebral blood volume and arterial blood pressure was poor.

This study has extended to man the observation previously made only in animals that cerebral blood volume is responsive to changes in arterial carbon dioxide tension. It has also been examined for the first time the regional responses of CBV to alterations in PaCO2. We have demonstrated that grey matter and white matter have the same sensitivities to carbon dioxide although they have different resting local blood volumes. The data generated in this study are being used as a normal baseline with which local cerebral blood volumes in various pathological conditions can be compared.

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Erratum
In the article by Robert E. Mates, Ramji L. Gupta, Adam C. Bell, and Francis J. Klocke, “Fluid Dynamics of Coronary Artery Stenosis,” Circ Res 42: 152-162 (January), 1978, in paragraph 1, page 152, the statement, “approximately 80-84%” should read “approximately 84-96%.” In the last sentence on page 153, the statement should read “the basic frequency of the system which is proportional to the heart rate.” The authors are grateful to Dr. Robert L. Feldman of the University of Florida for pointing out these errors.
Local cerebral blood volume response to carbon dioxide in man.
J H Greenberg, A Alavi, M Reivich, D Kuhl and B Uzzell

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